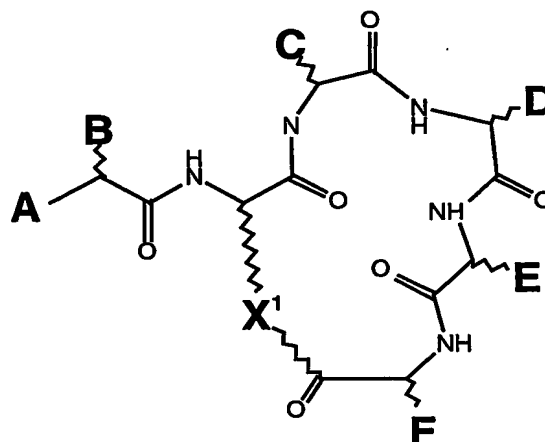


CLAIMS

1. A method of treatment of osteoarthritis,  
comprising the step of administering an effective amount  
5 of an inhibitor of a G protein-coupled receptor to a  
subject in need of such treatment, in which the inhibitor  
is a compound which  
(a) is an antagonist of a G protein-coupled receptor,  
(b) has substantially no agonist activity, and  
10 (c) is a cyclic peptide or peptidomimetic compound of  
formula I



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where A is H, alkyl, aryl,  $\text{NH}_2$ , NH-alkyl,  $\text{N}(\text{alkyl})_2$ , NH-aryl, NH-acyl, NH-benzoyl,  $\text{NHSO}_3$ ,  $\text{NHSO}_2$ -alkyl,  $\text{NHSO}_2$ -aryl, OH, O-alkyl, or O-aryl;

20 B is an alkyl, aryl, phenyl, benzyl, naphthyl or indole group, or the side chain of a D- or L-amino acid, but is not the side chain of glycine, D-phenylalanine, L-homophenylalanine, L-tryptophan, L-homotryptophan, L-tyrosine, or L-homotyrosine;

25 C is the side chain of a D-, L- or homo-amino acid, but is not the side chain of isoleucine, phenylalanine, or cyclohexylalanine;

D is the side chain of a neutral D-amino acid, but is not the side chain of glycine or D-alanine, a bulky planar side chain, or a bulky charged side chain;

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E is a bulky substituent, but is not the side chain of D-tryptophan, L-N-methyltryptophan, L-homophenylalanine, L-2-naphthyl L-tetrahydroisoquinoline, L-cyclohexylalanine, D-leucine, L-fluorenylalanine, or L-histidine;

F is the side chain of L-arginine, L-homoarginine, L-citrulline, or L-canavanine, or a bioisostere thereof; and

X is  $-(CH_2)_nNH-$  or  $(CH_2)_nS-$ , where n is an integer of from 1 to 4;  $-(CH_2)_2O-$ ;  $-(CH_2)_3O-$ ;  $-(CH_2)_3-$ ;  $-(CH_2)_4-$ ;  $-CH_2COCHRNH-$ ; or  $-CH_2-CHCOCHRNH-$ , where R is the side chain of any common or uncommon amino acid.

2. A method according to claim 1, in which n is 2 or 3.

15 3. A method according to claim 1 or claim 2, in which A is an acetamide group, an aminomethyl group, or a substituted or unsubstituted sulphonamide group.

4. A method according to claim 3, in which A is a substituted sulphonamide, and the substituent is an alkyl chain of 1 to 6 carbon atoms, or a phenyl or toluyl group.

5. A method according to claim 4, in which the substituent is an alkyl chain of 1 to 4 carbon atoms.

6. A method according to any one of claims 1 to 5, in which B is the side chain of L-phenylalanine or L-phenylglycine.

7. A method according to any one of claims 1 to 6, in which C is the side chain of glycine, alanine, leucine, valine, proline, hydroxyproline, or thioproline.

8. A method according to any one of claims 1 to 7, in which D is the side chain of D-Leucine, D-homoleucine, D-cyclohexylalanine, D-homocyclohexylalanine, D-valine, D-norleucine, D-homo-norleucine, D-phenylalanine, D-tetrahydroisoquinoline, D-glutamine, D-glutamate, or D-tyrosine.

35 9. A method according to any one of claims 1 to 8, in which E is the side chain of an amino acid selected from the group consisting of L-phenylalanine, L-tryptophan

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and L-homotryptophan, or is L-1-naphthyl or L-3-benzothienyl alanine.

10. A method according to any one of claims 1 to 9,  
in which the inhibitor is a compound which has antagonist  
5 activity against C5aR, and has no C5a agonist activity.

11. A method according to any one of claims 1 to 10,  
in which the inhibitor has potent antagonist activity at  
sub-micromolar concentrations.

12. A method according to any one of claims 1 to 11,  
10 in which the compound has a receptor affinity  $IC_{50} < 25\mu M$ ,  
and an antagonist potency  $IC_{50} < 1\mu M$ .

13. A method according to any one of claims 1 to 12,  
in which the compound is selected from the group  
consisting of compounds 1 to 6, 10 to 15, 17, 19, 20, 22,  
15 25, 26, 28, 30, 31, 33 to 37, 39 to 45, 47 to 50, 52 to 58  
and 60 to 70 described in PCT/AU02/01427.

14. A method according to claim 13, in which the  
compound is compound 1 (AcF-[OP-DCha-WR]), compound 33  
(AcF-[OP-DPhe-WR]), compound 60 (AcF-[OP-DCha-FR]) or  
20 compound 45 (AcF-[OP-DCha-WCit]) described in  
PCT/AU02/01427.

15. A method according to any one of claims 1 to 14,  
in which the inhibitor is used in conjunction with one or  
more other agents for the treatment of osteoarthritis.

25 16. Use of a compound as defined in any one of claims  
1 to 14 in the manufacture of a medicament for the  
treatment of osteoarthritis.